A Possible Mechanism for Lignin Model Synthesis

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Abstract

A Possible Mechanism for Lignin Model Synthesis. Cheryl Loveless (University of Portland, Portland, Oregon 97203) Joe Bozell (National Renewable Energy Laboratory, Golden, Colorado 80401).

Lignin is a potentially valuable renewable resource. Making up 30% of the dry weight of wood, it is the second most abundant organic matter on the Earth. Lignin is considered a by-product of wood pulping. Because of its complex structure, lignin is difficult to turn into other usable products. Thus, the production of accurate and usable lignin models is important in renewable chemistry. Performing reactions on lignin is impractical. A similar reaction may be performed on a lignin model, the results of which can be easy to interpret. The better the lignin model, the more likely reactions using the model will apply to lignin. A new method of synthesizing lignin models using orthoesters has been investigated at the National Renewable Energy Laboratory. The method reacts orthoesters with phenols to produce a biphenyl lignin model. This method produces two products, only one of which is the desired lignin model. The mechanism of this synthesis was investigated by reacting the two products to determine if conversion is possible. The phenol, methyl guaiacol, was not present in one set of reactions and was in excess in another. The reactions were followed by HPLC to determine the relative concentrations and rates of formation. It was found that an equilibrium exists between the two products and the phenol.

Research Category (Please Circle)

ERULF: Physics Chemistry Biology Engineering Computer Science Other _____
CCI: Biotechnology Environmental Science Computing

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Introduction

The conversion of lignin into commercially viable products is a long researched problem. Considered a by-product of paper pulping, most lignin is not used for commercial purposes. Because lignin is an abundant organic matter, second only to cellulose, it is a promising renewable resource. A seemingly untapped natural resource, lignin poses a challenge scientists because of its complex structure. Lignin is a large, complex aromatic polymer. Unlike cellulose, which has glucose as its simple repeating unit, lignin does not have a simple unit. There are three primary units in lignin, guaiacol, syringol, and p-hydroxyphenol **1,2**. The units are linked together by ether and carbon-carbon bonds **1**. The random joining of units leads to a complex polymer.

In woody plants, lignin is a secondary cell wall component **2**. It gives strength to the structural elements and increases water impermeability **2,3**. Lignin strengthens the structural elements of plants by making an admixture with hemicellulose that forms a cementing material for cellulose fibrils **3**. Trees can synthesize lignin in response to stress or to attack **2**. The amount of lignin varies between species, accounting for between 15-36% of the dry weight of wood **2**. The large amount of lignin present on the Earth may allow for many future applications of lignin.

Lignin is commonly available in the black liquor generated from wood pulping **3**. The pulping process affects the chemical structure and reactivity of lignin creating additional hurdles for developing commercially valuable products **1,3**. Currently, lignin is being transformed into crude fuels **1**. It is also being used for products such as polymers, adhesives, and resins **3**. However, the potential of lignin remains untapped because of the complexity of its chemical structure.

The complexity and size of lignin makes it difficult to work with in the laboratory. Creating lignin models to simulate small pieces of lignin allows for better chemistry to be done. Reactions done with the models give us a better idea of what future use lignin may have. The chemistry performed on the models may lead to the creation of new products from lignin, such as plastics. Improving the model improves the likelihood of the reaction being applicable to lignin. Researchers at the National Renewable Energy Laboratory have developed a new method for synthesizing lignin models.

The new method focuses on the stereoselective arylation of cyclic orthoesters. This method begins with an alkene with a phenyl group attached. The alkene is turned into a diol. The diol then forms an orthoester. The orthoester is reacted with a Lewis acid, generally BF_3, and a phenol to form a biphenyl lignin model. The orthoester reaction yields two products, depending on the attacking site on the phenol. The desired product is O-arylation and the secondary product is C-arylation. The mechanism behind the formation of the two products is yet unknown.

This paper proposes a possible mechanism for the arylation of cyclic orthoesters during the synthesis of lignin models. In this work, the reactions from Bozell were repeated and follow by HPLC to study the timing of the reactions. Corresponding reactions on the final products were also performed and analyzed by HPLC and NMR.

Methods and Materials

All reactions were performed in airless conditions under Ar gas. HPLC and TLC were used to follow each reaction. Final products were analyzed using NMR.

Diol Synthesis

Ethyl cinnamate (10 mmol) and 4-methylmorpholine-N-oxide (12 mmol) is dissolved in acteone/H_2O (4:1) and degassed. The solution is treated with OsO_4 (0.05 mmol) and allowed to stir at room temperature overnight. The reaction is quenched with sodium hydrogen sulfite and allowed to stir under air. The crude product is purified using chromatography on Si gel.

Orthoester Synthesis

The ethyl cinnamate β-diol (4 mmol) is added to the reaction flask under a stream of Ar gas. The diol is dissolved in THF and degassed. Trimethylorthoacetate (4.8 mmol) is added and the reaction is cooled to –25^{o}C. Para-toluenesulfonic acid (0.02 mmol) is added and the reaction is allowed to warm to room temperature. The reaction stirs for 2 hours and is quenched with triethylamine. The crude product is purified on a short Si gel plug in a fritted funnel.

Lignin Model Synthesis

The ethyl cinnamate orthoester (2 mmol) is dissolved in dry, degassed CH_2Cl_2 and cooled to –78^{o}C. The methyl guaiacol (6 mmol) is added to the solution and allowed to stir. $BF_3{\cdot}OEt_2$ (2.2 mmol) is added drop wise to the solution and the reaction is allowed to stir at –78^{o}C for 60 minutes. The temperature is raised to –20^{o}C and the reaction is allowed to stir for 50-75 hours. The reaction is quenched with triethylamine and the crude product is purified using chromatography on Si gel.

Lignin Model Synthesis Modifications

Different Lewis acids can be used. $TiCl_4$ and $SnCl_4$ are used in place of $BF_3{\cdot}OEt_2$.

The reaction can be done with EtCN as the solvent.

After 70 hours the reaction is brought to room temperature and allowed to stir, then is quenched with triethylamine.

O-arylation Product Reactions

The O-arylation product (2 mmol) is dissolved in dry, degassed CH_2Cl_2, and cooled to –78°C. $BF_3{\cdot}OEt_2$ (6 mmol) is added drop wise and allowed to stir at –78°C for 60 min. The temperature is raised to –20°C and the reaction is allowed to stir for 72 hours. The solution is allowed to warm to room temperature and stirs for an additional 24 hours. The reaction is quenched with triethylamine and the crude product is purified using chromatography on Si gel.

The O-arylation product (2 mmol) is dissolved in dry, degassed CH_2Cl_2, and cooled to –78°C. Methyl guaiacol (6 mmol) is added and the solution is allowed to stir. $BF_3{\cdot}OEt_2$ (6 mmol) is added drop wise and allowed to stir at –78°C for 60 min. The temperature is raised to –20°C and the reaction is allowed to stir for 72 hours. The solution is allowed to warm to room temperature and stirs for an additional 24 hours. The reaction is quenched with triethylamine and the crude product is purified using chromatography on Si gel

C-arylation Product Reactions

The C-arylation product (2 mmol) is dissolved in dry, degassed CH_2Cl_2, and cooled to –78°C. $BF_3{\cdot}OEt_2$ (6 mmol) is added drop wise and allowed to stir at –78°C for 60 min. The temperature is raised to –20°C and the reaction is allowed to stir for 72 hours. The solution is allowed to warm to room temperature and stirs for an additional 24 hours. The reaction is quenched with triethylamine and the crude product is purified using chromatography on Si gel.

The C-arylation product (2 mmol) is dissolved in dry, degassed CH_2Cl_2, and cooled to –78°C. Methyl guaiacol (6 mmol) is added and the solution is allowed to stir. $BF_3 \cdot OEt_2$ (6 mmol) is added drop wise and allowed to stir at –78°C for 60 min. The temperature is raised to –20°C and the reaction is allowed to stir for 72 hours. The solution is allowed to warm to room temperature and stirs for an additional 24 hours. The reaction is quenched with triethylamine and the crude product is purified using chromatography on Si gel

HPLC Analysis

HPLC was performed using a Waters 2690 Separations Module, a Waters 996 Photodiode Array Detector, and a Waters 2410 Refractive Index Detector. Resulting plots were analyzed using Millennium32 Software – Review. The wavelength is set to 280.1 nm, and the peaks are integrated. Integration parameters are peak width = 150, threshold = 300, minimum area = 0, minimum height = 0.

NMR Analysis

^1H NMR was performed using a Varian Unity 30000. The samples are dissolved in $CDCl_3$, which is used as an internal standard.

Results

The investigation was successful in producing lignin models. Two products, C-arylation and O-arylation were formed, as confirmed by NMR. When the reaction was done in CH_2Cl_2 and was kept at –20°C, the C-arylation to O-arylation final product ratio was 38/36.

The BF_3 orthoester reactions were followed by HPLC. Figure 1 shows a typical HPLC trace and integration. The HPLC is representative of the reaction from the addition of BF3 until the reaction is quenched. The peak at 4.3 is methyl guaiacol, the peak at 7.5 is C-arylation, and

the peak at 10.8 is O-arylation. Over time, the relative peak intensity changes, as shown is Figure 2.

The HPLC traces of the O-arylation reaction are shown in Figure 3. At the end of the reaction, methyl guaiacol, C-arylation, and O-arylation are present.. The final percent yield of methyl guaiacol is 3, of O-arylation is 14, and of C-arylation is 19. NMR analysis of C-arylation and O-arylation shows slightly different peaks and/or peak heights from standards.

The HPLC traces of the O-arylation methyl guaiacol reaction are show in Figure 4. C-arylation, O-arylation, and methyl guaiacol are present at the end of the reaction. The final percent yield of O-arylation is 48 and of C-arylation is 9. NMR analysis shows that the O-arylation product is identical to the starting material. The C-arylation product is slightly different from the C-arylation standard.

Figure 5 shows the HPLC traces for the C-arylation reaction. Only C-arylation is present at the end of the reaction. Further analysis of the reaction was not possible. Figure 6 shows the HPLC traces for the C-arylation methyl guaiacol reaction. At the end of the reaction, methyl guaiacol, C-arylation, and O-arylation are present. Further analysis was not possible.

Performing the orthoester BF_3 reaction in EtCN led to the production of C-arylation and O-arylation. C-arylation was the dominant product with a making up 67% of the final product weight. O-arylation made up 8% of the final product weight. When the reaction was performed in CH_2Cl_2 and allowed to come to room temperature, C-arylation was the dominant product. Reacting the orthoester with $TiCl_4$ and $SnCl_4$ produced many products. Isolation of C-arylation and O-arylation was not possible.

Discussion and Conclusions

The formation of the desired lignin model, O-arylation, is most successful using CH_2Cl_2 as a solvent and BF_3 as a Lewis acid. Other Lewis acids and solvents produce O-arylation, but not in desirable quantities. Keeping the reaction at –20°C for 72 hours optimizes the amount of O-arylation produced. Raising the reaction temperature to room temperature produces more C-arylation than O-arylation.

Following the BF_3 orthoester reaction over time, Figure 3, shows that both the C-arylation and O-arylation products are formed immediately following the addition of BF_3. After 4 hours, the reaction seems to reach a steady state. While the relative amount of methyl guaiacol continues to decrease, the ratio between C-arylation and O-arylation remains steady. For the next few days, the relative concentrations of C-arylation and O-arylation do not change, with O-arylation being the dominant product. Once the reaction is brought to room temperature, C-arylation becomes the dominant product. This inversion does not occur when the reaction is kept at –20°C over the same period of time. This inversion lead to the BF_3 reactions with the products to determine if the O-arylation was turning in C-arylation, or if more of the orthoester was reacting and turning into C-arylation only. In addition, the relative amount of methyl guaiacol to O-arylation increases. This suggests that the amount of O-arylation present in the reaction is decreasing. This points to the possibility that O-arylation is being converted to C-arylation.

The HPLC traces, Figure 3, of the O-arylation BF_3 reaction show that the reaction does not proceed at –78°C or –20°C. This is in sharp contrast to the BF_3 orthoester reaction, in which products are formed immediately. Once the reaction is raised to room temperature, C-arylation and methyl guaiacol begin to form. When the reaction is quenched, there is more C-arylation than O-arylation present and there is a small amount of methyl guaiacol present. This shows that

O-arylation can convert to C-arylation and methyl guaiacol at room temperature. While the orthoester may continue to react with BF_3 at room temperature, the change in relative concentrations, as seen in Figure 2, may be due to the conversion of O-arylation to C-arylation.

When an excess of methyl guaiacol is added to the O-arylation BF_3 reaction, different results are obtained. Again, the reaction does not proceed at -78^oC or at -20^oC. In contrast to the reaction without methyl guaiacol, very little C-arylation is formed at room temperature. This suggests that an equilibrium is set up between O-arylation and C-arylation plus methyl guaiacol. When an excess of methyl guaiacol is present, the equilibrium follows Le Chatlier's principle and shifts to the O-arylation to try to balance the stress. This is why we see small amounts of C-arylation formed when an excess of methyl guaiacol is added. In the orthoester BF_3 reaction, the excess of methyl guaiacol is likely less than the excess used in the O-arylation reaction. This may allow for some of the O-arylation to convert to C-arylation.

The C-arylation BF_3 reactions appear to confirm that an equilibrium exists between the two products and methyl guaiacol. When only C-arylation is present, O-arylation is not formed. Because the methyl guaiacol is absent, the equilibrium can not set up, prohibiting the formation of O-arylation. When methyl guaiacol is present, as in Figure 6, O-arylation is formed. This confirms that an equilibrium exists between C-arylation, methyl guaiacol, and O-arylation, Figure 6. Further research is needed to confirm the mechanism. Varying the reaction times and temperatures may provide an idea as to when the equilibrium is reached during the orthoester BF_3 reaction.

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References

Thring, Ronald W.; Katikaneni, Sai P.R.; Bakhsi, Narendra N. The production of gasoline range hydrocarbons from Alcell lignin using HZSM-5 catalyst. *Fuel Processing Technology* **2000**, 62, 17-30.

Grima-Pettenati, Jacqueline; Goffner, Deborah Lignin genetic engineering revisited. *Plant Science*, **1999**, 145, 51-65.

Rohella, R.S.; Sahoo, N.; Paul, S.C.; Choudhury, S.; Chakravortty, V. Thermal studies on isolated and purified lignin. *Thermochimica Acta*, **1996**, 287, 131-138.

Figures

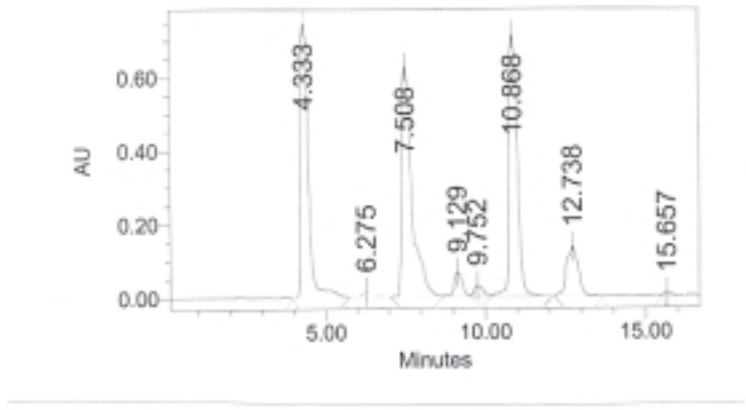

Figure 1. HPLC trace of a typical orthoester BF_3 reaction at –20°C

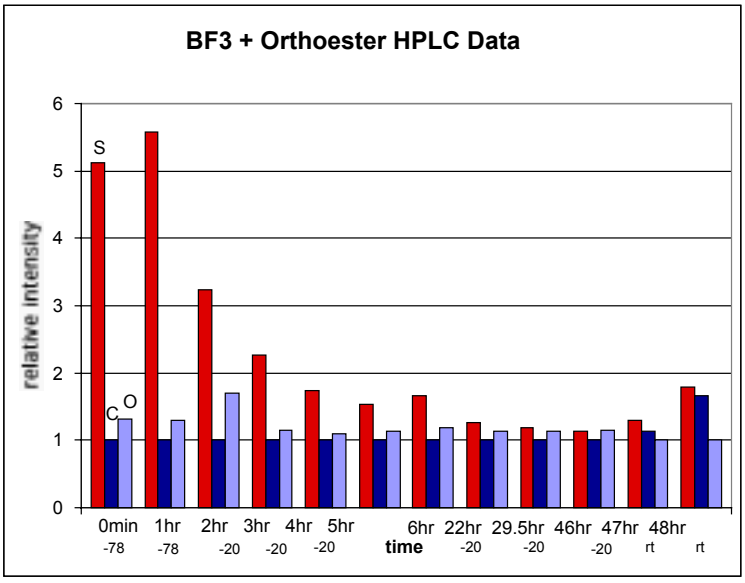

Figure 2. Relative peak intensities from HPLC traces of orthoester BF_3 reaction over time

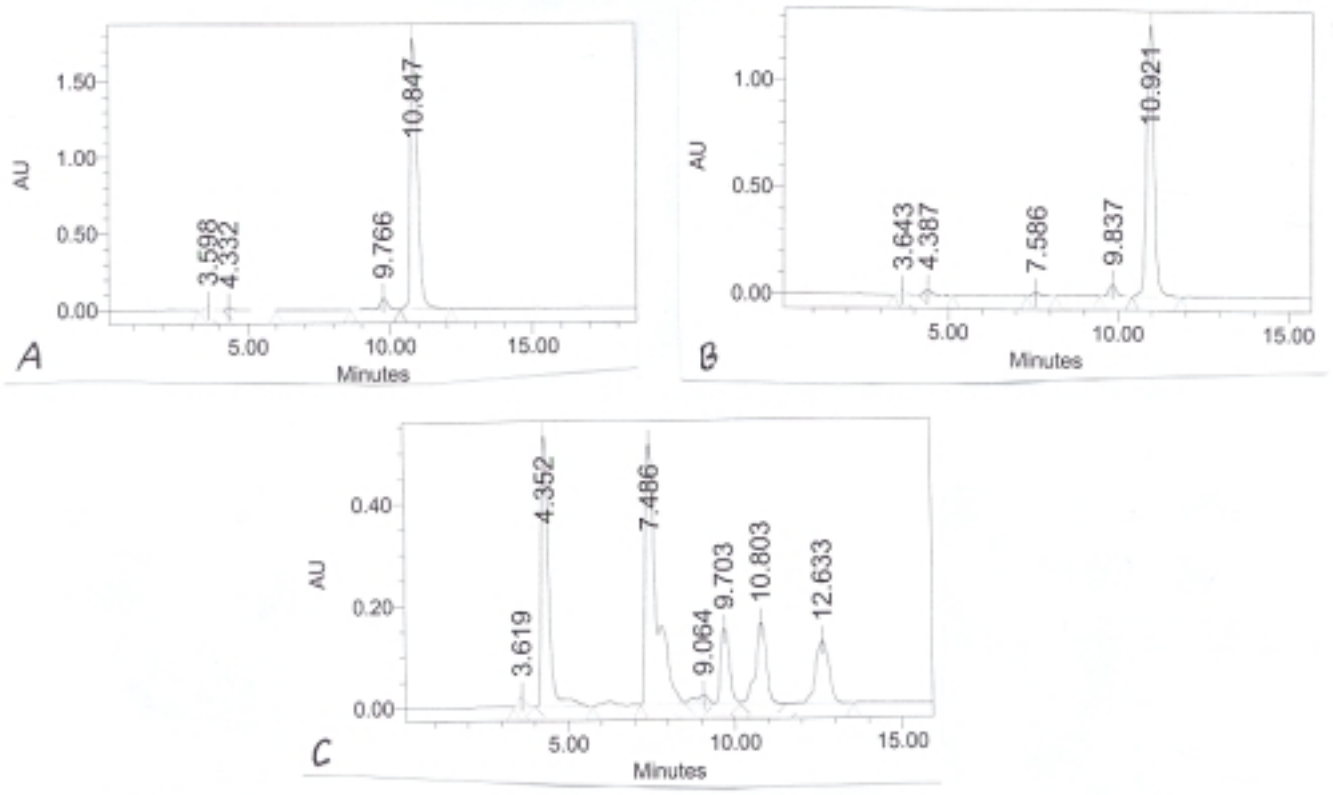

Figure 3. HPLC traces of an O-arylation BF3 reaction. A) 0 minuets, -78°C B) 72 hours, -20°C C) 96 hours, room temperature

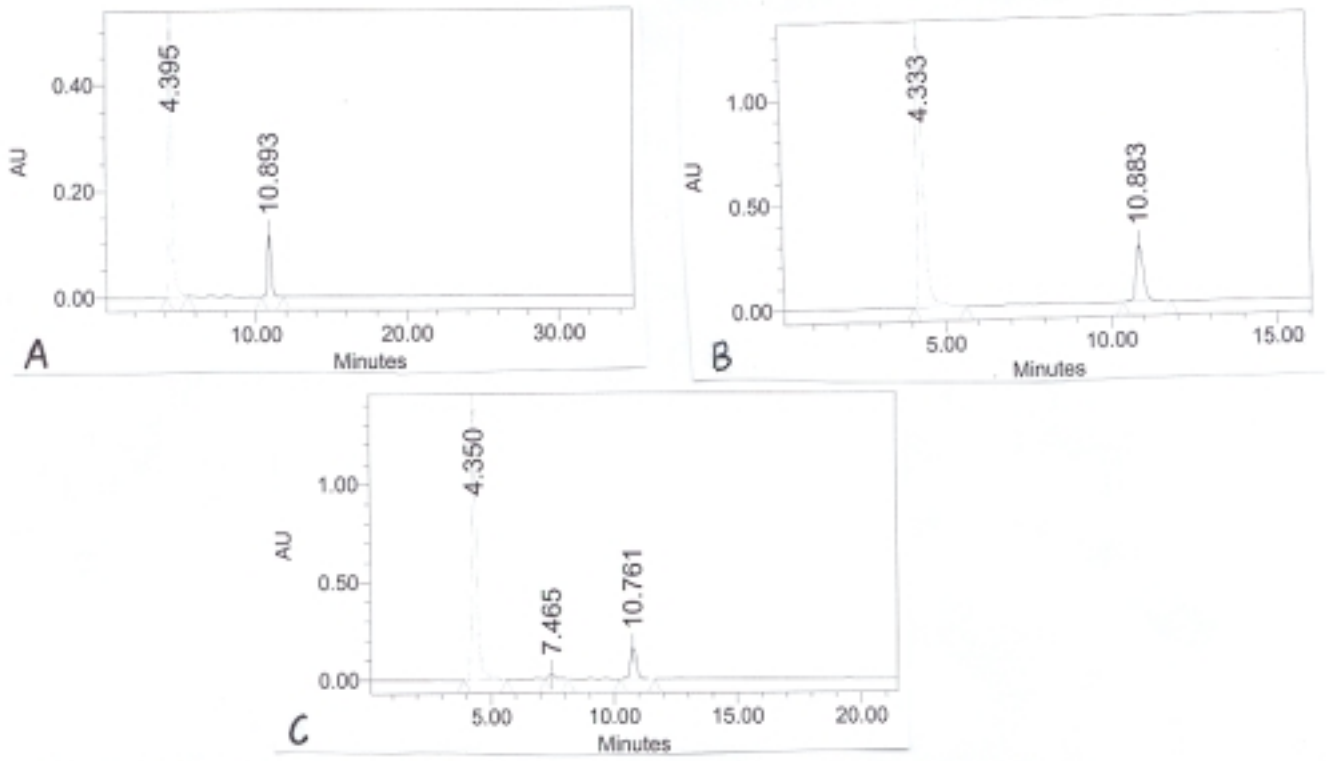

Figure 4. HPLC traces of an O-arylation and methyl guaiacol BF3 reaction. A) 0 minuets, -78°C B) 72 hours, -20°C C) 102 hours, room temperature

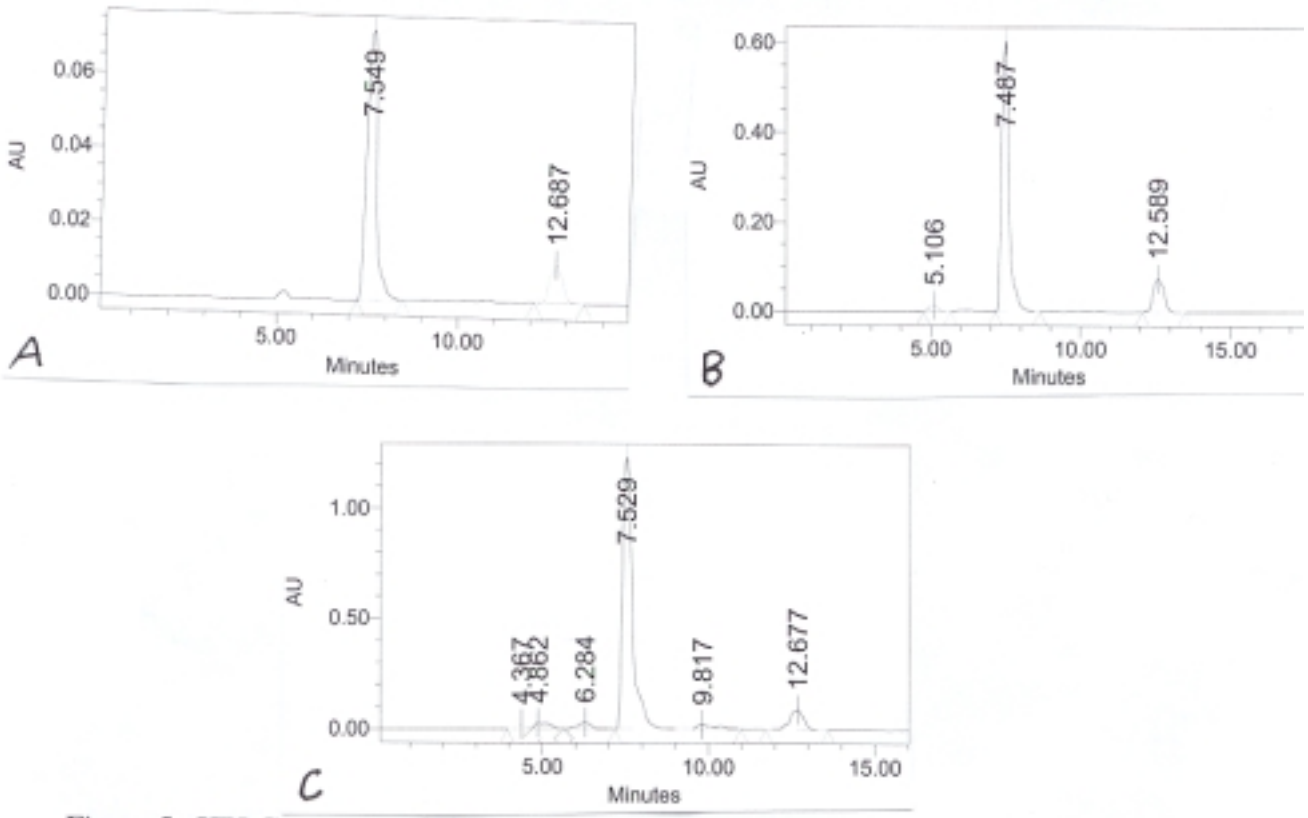

Figure 5. HPLC traces of an C-arylation BF3 reaction. A) 0 minuets, -78°C B) 72 hours, -20°C C) 96 hours, room temperature

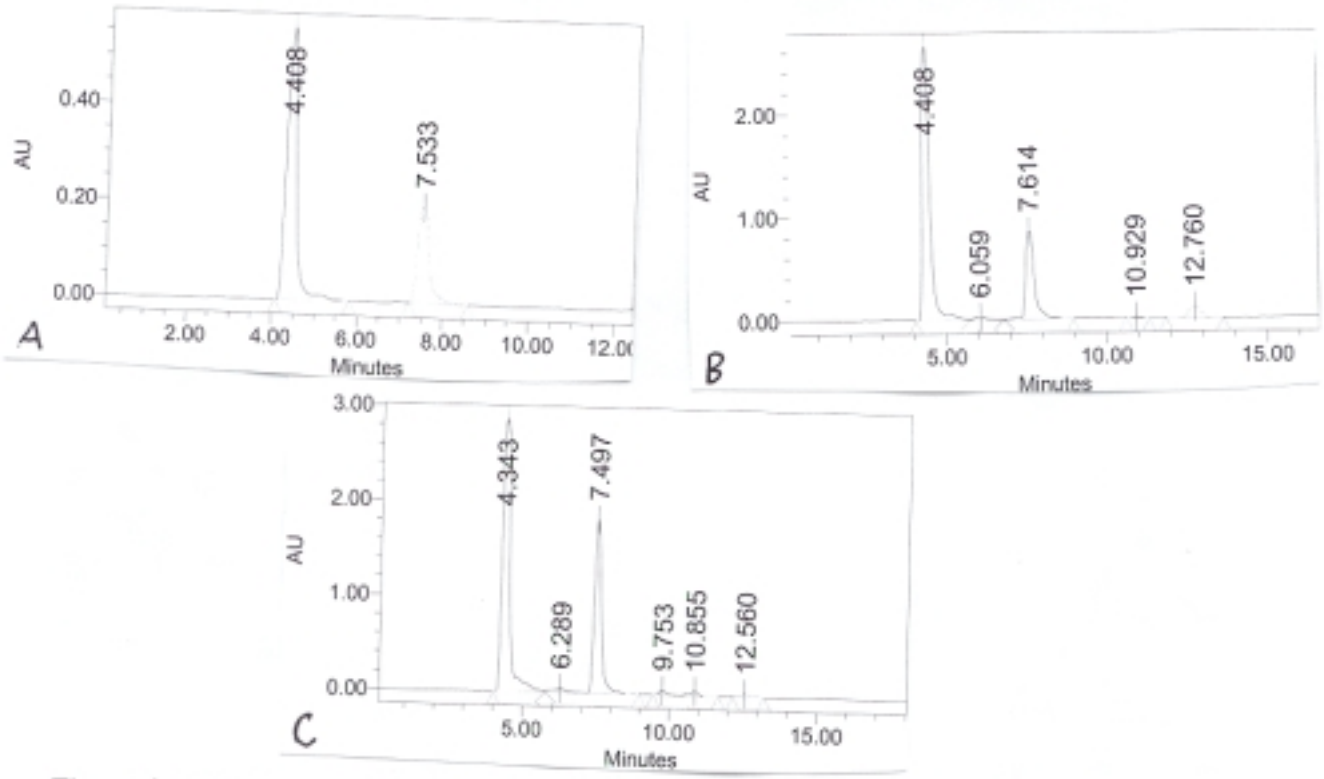

Figure 6. HPLC traces of an C-arylation and methyl guaiacol BF3 reaction. A) 0 minuets, -78°C B) 72 hours, -20°C C) 102 hours, room temperature

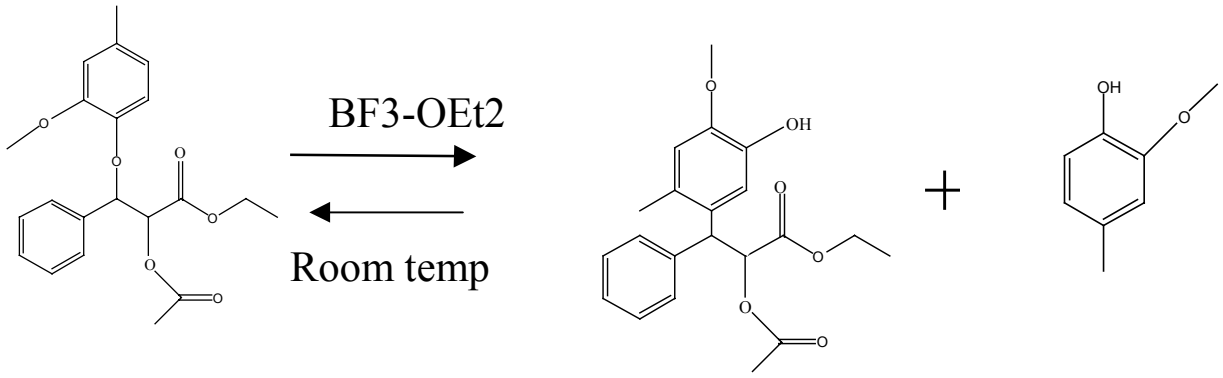

Figure 7. Possible mechanism for lignin model synthesis